

CLAIMS

What is claimed is:

1. A multispecific antibody comprising:
 - a) a first antigen-binding fragment that specifically binds CD3, wherein the first antigen-binding fragment is fused to a first masking moiety (MM1) via a first cleavable moiety (CM1) comprising a first cleavage site, wherein the first antigen-binding fragment comprises a first immunoglobulin light chain variable domain (VL1) and a first immunoglobulin heavy chain variable domain (VH1) of an anti-CD3 antibody, wherein the MM1 is fused to the N-terminus of the VL1 via the CM1, wherein the MM1 inhibits binding of the multispecific antibody to CD3 when the CM1 is not cleaved, and wherein the MM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, and 597-599 and the CM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431 and 477-490, and 516-555; and
 - b) a second antigen-binding fragment that specifically binds a target antigen; wherein the MM1 competes with CD3 to specifically bind the CD3-binding moiety; and wherein
 - i. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
 - ii. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
iii. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
iv. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
v. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
vi. the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

vii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 398,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 399, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

viii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

ix. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

x. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and

a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

xi. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;

xii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;

xiii. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381; or

xiv. the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,

a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,

a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and

a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381~~the first antigen-binding fragment fused to the MM1 binds CD3 with half-maximal binding at a concentration of antibody (EC_{50}) that is at least 10 nM as determined by an enzyme-linked immunosorbent assay (ELISA).~~

~~2. The multispecific antibody of claim 1, wherein the first antigen-binding fragment binds CD3 with a dissociation constant (K_d) of at least 100 nM.~~

~~3. The multispecific antibody of claim 1 or 2, wherein the MM1 has a masking efficiency of at least 50 as determined by a Jurkat NFAT reporter assay.~~

~~4. The multispecific antibody of any one of claims 1-3, wherein the first antigen-binding fragment is selected from the group consisting of a Fab, a Fv, a scFab and a scFv.~~

~~5. The multispecific antibody of any one of claims 1-4, wherein the multispecific antibody is an activatable multispecific antibody.~~

~~6. The multispecific antibody of any one of claims 1-5, wherein the first antigen-binding fragment is fused to the MM1 via a first cleavable moiety (CM1);~~

~~wherein the CM1 comprises a first cleavage site;~~

~~wherein the MM1 inhibits binding of the multispecific antibody to CD3 when the CM1 is not cleaved; and~~

~~wherein the multispecific antibody binds CD3 via the first antigen-binding fragment with higher affinity when the CM1 is cleaved.~~

~~7. The multispecific antibody of any one of claims 1-6, wherein the first antigen-binding fragment comprises a first immunoglobulin light chain variable domain (VL1) and a first immunoglobulin heavy chain variable domain (VH1) of an anti-CD3 antibody, and wherein the MM1 is fused to the N-terminus of the VL1 via the CM1.~~

28. The multispecific antibody of claim 17, wherein the first antigen-binding fragment is a scFv comprising, from N-terminus to C-terminus, VL1, a linker, and VH1.

39. The multispecific antibody of claim 28, wherein the multispecific antibody comprises a first polypeptide, a second polypeptide, and a third polypeptide, wherein:

(i) the first polypeptide comprises a structure represented by the formula:

VH2-CH1-hinge-CH2-first CH3 (1a);

(ii) the second polypeptide comprises a structure represented by the formula:

MM1-CM1-VL1-VH1-hinge-CH2-second CH3 (1b); and

(iii) the third polypeptide comprises a structure represented by the formula:

VL2-CL (1c);

wherein:

CL is an immunoglobulin light chain constant domain;

CH1 is an immunoglobulin heavy chain constant domain 1;

CH2 is an immunoglobulin heavy chain constant domain 2;

first CH3 is a first immunoglobulin heavy chain constant domain 3;

second CH3 is a second immunoglobulin heavy chain constant domain 3;

hinge is an immunoglobulin hinge region connecting the CH1 and CH2 domains;

wherein the VL1 and the VH1 associate to form a scFv that specifically binds CD3; and

wherein the VL2 and the VH2 associate to form a Fv that specifically binds the target antigen.

~~10. The multispecific antibody of any one of claims 1-4, wherein the multispecific antibody does not comprise a cleavable linker.~~

~~11. The multispecific antibody of any one of claims 1-4 and 10, wherein the first antigen-binding fragment comprises a first immunoglobulin light chain variable domain (VL1) and a first immunoglobulin heavy chain variable domain (VH1) of an anti-CD3 antibody, and wherein the MM1 is fused to the N-terminus of the VL1 via a first non-cleavable linker (NCL1).~~

~~12. The multispecific antibody of claim 11, wherein the first antigen-binding fragment is a scFv comprising, from N-terminus to C-terminus, VL1, a linker, and VH1.~~

~~13. The multispecific antibody of claim 12, wherein the multispecific antibody comprises a first polypeptide, a second polypeptide, and a third polypeptide, wherein:~~

~~(i) the first polypeptide comprises a structure represented by the formula:~~

~~VH2-CH1-hinge-CH2-first CH3 (1a);~~

~~(ii) the second polypeptide comprises a structure represented by the formula:~~

~~MM1-NCL1-VL1-VH1-hinge-CH2-second CH3 (1b); and~~
~~(iii) the third polypeptide comprises a structure represented by the formula:~~

~~VL2-CL (1c);~~

~~wherein:~~

~~CL is an immunoglobulin light chain constant domain;~~

~~CH1 is an immunoglobulin heavy chain constant domain 1;~~

~~——CH2 is an immunoglobulin heavy chain constant domain 2;~~

~~——first CH3 is a first immunoglobulin heavy chain constant domain 3;~~

~~——second CH3 is a second immunoglobulin heavy chain constant domain 3;~~

~~hinge is an immunoglobulin hinge region connecting the CH1 and CH2 domains;~~

~~wherein the VL1 and the VH1 associate to form a scFv that specifically binds CD3; and~~

~~wherein the VL2 and the VH2 associate to form a Fv that specifically binds the target antigen.~~

414. The multispecific antibody of ~~any one of claims 1-13~~claim 1, wherein the second antigen-binding fragment comprises a second immunoglobulin light chain variable domain (VL2) and a second immunoglobulin heavy chain variable domain (VH2) of an antibody that specifically binds the target antigen.

515. The multispecific antibody of claim 414, wherein the second antigen-binding fragment is selected from the group consisting of a Fab, a Fv, a scFab and a scFv.

616. The multispecific antibody of claim 515, wherein the second antigen-binding fragment is fused to a second masking moiety (MM2) via a second cleavable moiety (CM2), wherein the CM2 comprises a second cleavage site, wherein the MM2 inhibits binding of the multispecific antibody to the target antigen when the CM2 is not cleaved, and wherein the multispecific antibody binds the target antigen via the second antigen-binding fragment when the CM2 is cleaved.

717. The multispecific antibody of claim 616, wherein the MM2 is fused to the N-terminus of the VL2 via the CM2.

818. The multispecific antibody of claim 716 or 17, wherein the multispecific antibody comprises a first polypeptide, a second polypeptide, and a third polypeptide, wherein:

(i) the first polypeptide comprises a structure represented by the formula:

VH2-CH1-hinge-CH2-first CH3 (2a);

(ii) the second polypeptide comprises a structure represented by the formula:

MM1-VL1-VH1-hinge-CH2-second CH3 (2b); and

(iii) the third polypeptide comprises a structure represented by the formula:

MM2-CM2-VL2-CL (2c);

wherein:

CL is an immunoglobulin light chain constant domain;

CH1 is an immunoglobulin heavy chain constant domain 1;

CH2 is an immunoglobulin heavy chain constant domain 2;

first CH3 is a first immunoglobulin heavy chain constant domain 3;

second CH3 is a second immunoglobulin heavy chain constant domain 3;

hinge is an immunoglobulin hinge region connecting the CH1 and CH2 domains;

wherein the VL1 and the VH1 associate to form a scFv that specifically binds CD3; and

wherein the VL2 and the VH2 associate to form a Fv that specifically binds the target antigen.

~~919.~~ The multispecific antibody of ~~any one of claim 1-18~~claim 1, wherein the CD3 is human CD3.

~~20.~~ ~~The multispecific antibody of claim 19, wherein the first antigen binding fragment is cross reactive with a CD3 polypeptide from at least one non human species selected from the group consisting of cynomolgus monkey, mouse, rat and dog.~~

~~21.~~ ~~The multispecific antibody of any one of claims 1-20, wherein the first antigen binding fragment comprises a VH1 and a VL1 of an anti-CD3 antibody, and wherein:~~

~~a) the VH1 comprises~~

~~a CDR-H1 comprising the amino acid sequence according to Formula (I): $X_1YAX_2X_3$ (SEQ ID NO: 382), wherein X_1 is D, S, or T, X_2 is I, L, or M, and X_3 is N or T;~~

~~a CDR-H2 comprising the amino acid sequence according to Formula (II):~~

~~$RIRSKYNNYATYYAX_1X_2VKX_3$ (SEQ ID NO: 383), wherein X_1 is D or E, X_2 is S or T, and X_3 is D, G, or S, and~~

~~a CDR-H3 comprising the amino acid sequence according to Formula (III):~~

~~$HGNX_1GX_2SYVSX_3X_4AY$ (SEQ ID NO: 384), wherein X_1 is F or Y, X_2 is N or T, X_3 is W or Y, and X_4 is F or W; and~~

~~b) the VL1 comprises~~

- a CDR-L1 comprising the amino acid sequence according to Formula (IV):
 X_1 SSTGAVTX₂X₃NYX₄N (SEQ ID NO: 385), wherein X₁ is A, G, or R, X₂ is S or T, X₃ is G or S, and X₄ is A, P, or V;
- a CDR-L2 comprising the amino acid sequence according to Formula (V):
 GTX₁X₂RAP (SEQ ID NO: 386), wherein X₁ is K or N, and X₂ is F or K, and
- a CDR-L3 comprising the amino acid sequence according to Formula (VI):
 ALWYSX₁X₂WV (SEQ ID NO: 387), wherein X₁ is D, N, or T, and X₂ is L or R.
22. ~~—The multispecific antibody of any one of claims 1–21, wherein:~~
- a) ~~the VH1 comprises~~
- a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376, 390, 601, and 602, or a variant thereof comprising up to about 3 amino acid substitutions;
- a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 377, 391–394, and 603, or a variant thereof comprising up to about 3 amino acid substitutions; and
- a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378, 395, 604, and 605, or a variant thereof comprising up to about 3 amino acid substitutions; and
- b) ~~the VL1 comprises~~
- a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396–398, and 606–609, or a variant thereof comprising up to about 3 amino acid substitutions;
- a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, or a variant thereof comprising up to about 3 amino acid substitutions; and
- a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, 400–401, and 610, or a variant thereof comprising up to about 3 amino acid substitutions.
23. ~~—The multispecific antibody of claim 22, wherein:~~
- a) ~~the VH1 comprises~~

- a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376 and 390, or a variant thereof comprising up to about 3 amino acid substitutions;
 - a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 391-394, or a variant thereof comprising up to about 3 amino acid substitutions; and
 - a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378 and 395, or a variant thereof comprising up to about 3 amino acid substitutions; and
- b) ~~the VL1 comprises~~
- a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396-398, or a variant thereof comprising up to about 3 amino acid substitutions;
 - a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, or a variant thereof comprising up to about 3 amino acid substitutions; and
 - a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, and 400-401, or a variant thereof comprising up to about 3 amino acid substitutions.
24. ~~The multispecific antibody of any one of claims 21-23, wherein:~~
- a) ~~the VH1 comprises~~
- a CDR-H1 comprising ~~the amino acid sequence of~~ SEQ ID NO: 376;
 - a CDR-H2 comprising ~~the amino acid sequence of~~ SEQ ID NO: 391; and
 - a CDR-H3 comprising ~~the amino acid sequence of~~ SEQ ID NO: 378; and
- ~~the VL1 comprises~~
- a CDR-L1 comprising ~~the amino acid sequence of~~ SEQ ID NO: 396;
 - a CDR-L2 comprising ~~the amino acid sequence of~~ SEQ ID NO: 380; and
 - a CDR-L3 comprising ~~the amino acid sequence of~~ SEQ ID NO: 381;
- b) ~~the VH1 comprises~~
- a CDR-H1 comprising ~~the amino acid sequence of~~ SEQ ID NO: 390;
 - a CDR-H2 comprising ~~the amino acid sequence of~~ SEQ ID NO: 392; and

- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
- e) the VH1 comprises
- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
- the VL1 comprises
- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
- d) the VH1 comprises
- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
- the VL1 comprises
- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
- e) the VH1 comprises
- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
- the VL1 comprises
- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;
- f) the VH1 comprises
- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,

- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
- g) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 398,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 399, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
- h) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
- i) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
- j) the VH1 comprises

- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~k) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~
- ~~l) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~m) the VH1 comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and
the VL1 comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381; or~~

n) ~~the VH1 comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~

~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~

~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~

~~the VL1 comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~

~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~

~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.~~

1025. The multispecific antibody of claim 124, wherein the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,

a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and

a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,

a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and

a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400.

1126. The multispecific antibody of claim 124, wherein the VH1 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,

a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and

a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and

the VL1 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,

a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and

a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.

1227. The multispecific antibody of ~~any one of claims 1-26~~claim 1, wherein the first antigen-binding fragment comprises a VH1 and a VL1, and wherein:

a) the VH1 comprises the amino acid sequence according to Formula (VII):

EVQLVESGGGLVX₁PGGSLRLSCAASGFTFX₂X₃YAIX₄WVRQAPGKGLEWVX₅RI
RSKYNNYATYYAX₆SVKX₇RFTISRDX₈SKNTLYLQX₉NSLRAEDTAVYYCX₁₀RH
GNX₁₁GX₁₂SYVSWFAYWGQGTLVTVSS (SEQ ID NO: 388), wherein X₁ is K or Q,

X₂ is N or S, X₃ is S or T, X₄ is H or N, X₅ is G or S, X₆ is D or E, X₇ is D or G, X₈ is D or N, X₉ is I or L, X₁₀ is A or V, X₁₁ is F or Y, X₁₂ is N or T; and

- b) the VL1 comprises the amino acid sequence according to Formula (VIII):

X₁AVVTQEPSTLVSPGGTVTLTCX₂SSTGAVTTSNYX₃NWX₄QQKPGQAPRGLIGGTX₅X₆RAPGX₇PARFSGSLLGGKAALTLGAQPEDEAEYYCALWYSX₈X₉WVFGGGTKLTVL (SEQ ID NO: 389), wherein X₁ is E or Q, X₂ is A, G, P, or R, X₃ is A or P, X₄ is F or V, X₅ is K or N, X₆ is F or K, X₇ is A, I, T, or V, X₈ is A, D, N, or T, and X₉ is H or L.

~~28. The multispecific antibody of claim 27, wherein the VH1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640, or a variant thereof having at least about 80% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640; and the VL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666, or a variant thereof having at least about 80% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666.~~

~~29. The multispecific antibody of claim 27, wherein the VH1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414, 415, and 416; and the VL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, and 413.~~

1330. The multispecific antibody of ~~any one of claims 27-29~~claim 12, wherein:

- a) the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403;
- b) the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises the amino acid sequence of SEQ ID NO: 404;
- c) the VH1 comprises the amino acid sequence of SEQ ID NO: 405, and the VL1 comprises the amino acid sequence of SEQ ID NO: 406;
- d) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 404;
- e) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403;

- f) the VH1 comprises the amino acid sequence of SEQ ID NO: 407, and the VL1 comprises the amino acid sequence of SEQ ID NO: 408;
- g) the VH1 comprises the amino acid sequence of SEQ ID NO: 409, and the VL1 comprises the amino acid sequence of SEQ ID NO: 408;
- h) the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411;
- i) the VH1 comprises the amino acid sequence of SEQ ID NO: 412, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
- j) the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
- k) the VH1 comprises the amino acid sequence of SEQ ID NO: 414, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403;
- l) the VH1 comprises the amino acid sequence of SEQ ID NO: 415, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413;
- m) the VH1 comprises the amino acid sequence of SEQ ID NO: 416, and the VL1 comprises the amino acid sequence of SEQ ID NO: 413; or
- n) the VH1 comprises the amino acid sequence of SEQ ID NO: 416, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411.

1431. The multispecific antibody of claim 1330, wherein the VH1 comprises the amino acid sequence of SEQ ID NO: 402, and the VL1 comprises the amino acid sequence of SEQ ID NO: 403.

1532. The multispecific antibody of claim 1330, wherein the VH1 comprises the amino acid sequence of SEQ ID NO: 410, and the VL1 comprises the amino acid sequence of SEQ ID NO: 411.

~~33. The multispecific antibody of any one of claims 28-32, wherein the first antigen-binding fragment comprises the amino acid sequence of SEQ ID NO: 421 or SEQ ID NO: 422.~~

~~34. The multispecific antibody of any one of claims 1-33, wherein the MM1 comprises:~~

- ~~a) the amino acid sequence of EVGSY (SEQ ID NO: 667) at the N-terminus of the MM1; or~~
- ~~b) an amino acid sequence according to Formula (IX): PYDDPDCPSHX₁SDCDX₂ (SEQ ID NO: 668), wherein X₁ is D or E, and X₂ is N or Q.~~

~~35. — The multispecific antibody of claim 34, wherein the MM1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, and 597-599.~~

1636. The multispecific antibody of claim 135, wherein the MM1 comprises the amino acid sequence of SEQ ID NO: 417.

1737. The multispecific antibody of ~~any one of claims 6-9 and 14-36~~claim 1, wherein the CM1 comprises ~~an the~~ amino acid sequence ~~selected from the group consisting of~~ SEQ ID NOs: 77, 127-129, 418, 420, 431 and 477-490, and 516-555.

1838. The multispecific antibody of claim 137, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: ~~77 or~~ 418.

~~39. — The multispecific antibody of any one of claims 1-38, wherein the target antigen is a tumor antigen.~~

~~40. — The multispecific antibody of claim 39, wherein the tumor antigen is selected from the group consisting of CD19, CD20, EpCAM, CEA, PSMA, CD33, EGFR, HER2, EphA2, MCSP, ADAM17, PSCA, 17-A1, NKG2D, TROP2, CD79B, Nectin-4, BCMA, CD22, CD38, EGFR, GD2, SLAMF7, CD30, EpCAM, MUC1, MUC16, CD123, CD37, FOLR1, MET, FLT3, GPC3, CEACAM5, CLDN18, CSF1, Integrin alpha-5, NCAM1, PTPRC, CD138, NaPi2b, MSLN, DLL3, GPRC5D, GPNMB, ICAM1, SSTR2, carcinoma-associated antigen CTAA16, CA9, ENG, ACVRL1, CD80, CSPG4, EGFL7, FLT1, HAVCR1, HGF, HLA-DRB, IGF1R, TPBG, ERBB3, and STEAP2.~~

1941. The multispecific antibody of claim 140, wherein the target antigen is HER2.

2042. The multispecific antibody of claim 1941, wherein the second antigen-binding fragment comprises a VH2 and a VL2 of an anti-HER2 antibody, and wherein:

the VH2 comprises

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 423,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 424, and
- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71; and

the VL2 comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 72,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 73, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 74.

2143. The multispecific antibody of claim 2042, wherein the VH2 comprises the amino acid sequence of SEQ ID NO: 75, and the VL2 comprises the amino acid sequence of SEQ ID NO: 76.

2244. The multispecific antibody of ~~any one of claims 41-43~~claim 20, wherein:

a) the MM2 comprises an amino acid sequence according to Formula (XI):

ESX₁X₂CX₃X₄DPFX₅CQX₆ (SEQ ID NO: 670), wherein X₁ is D or E, X₂ is A, F, V, or Y, X₃ is D or E, X₄ is A or L, X₅ is D or E, and X₆ is A, F, or Y;

b) the MM2 comprises an amino acid sequence according to Formula (XII):

X₁X₂X₃X₄X₅X₆CX₇X₈DPYECX₉X₁₀ (SEQ ID NO: 671), wherein X₁ is A, H, or S, X₂ is A, D, or S, X₃ is A, T, or V, X₄ is P, S, or T, X₅ is D or E, X₆ is A or V, X₇ is D or E, X₈ is A or L, X₉ is Q, S, or T, and X₁₀ is A, H, or V; or

c) the MM2 comprises an amino acid sequence according to Formula (XIII):

YNSDDDCX₁SX₂YDPYTCYY (SEQ ID NO: 672), wherein X₁ is A, I, or V, and X₂ is H or R.

2345. The multispecific antibody of ~~any one of claims 41-44~~claim 20, wherein the MM2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 36, 419, 432-476 and 491-515.

2446. The multispecific antibody of claim 2345, wherein the MM2 comprises the amino acid sequence of SEQ ID NO: 419.

2547. The multispecific antibody of ~~any one of claims 41-46~~claim 24, wherein the CM2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431, 477-490, and 516-555.

2648. The multispecific antibody of claim 2547, wherein the CM2 comprises the amino acid sequence of SEQ ID NO: 77 or 420.

2749. The multispecific antibody of ~~any one of claims 41-48~~claim 26, comprising:

- a) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 425,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 426, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 112;

- b) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 427,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 428, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 112;
- c) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 429,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 430, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 115;
- d) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 83,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 84, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 85;
- e) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 683,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 684, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 685;
- f) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 425,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 426, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
- g) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
- h) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 429,

- a second polypeptide comprising the amino acid sequence of SEQ ID NO: 430, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 115;
- i) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85;
 - j) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685;
 - k) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 425 without the
C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 426 without
the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
 - l) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427 without the
C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428 without
the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;
 - m) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 429 without the
C-terminal lysine,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 430 without
the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 115;
 - n) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84 without the
C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85 without the
C-terminal lysine; or
 - o) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684 without
the C-terminal lysine, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685 without the C-terminal lysine.

2850. The multispecific antibody of claim 140, wherein the target antigen is CD20.

2951. The multispecific antibody of claim 2850, wherein the second antigen-binding fragment comprises a VH2 and a VL2 of an anti-CD20 antibody, and wherein:

a) the VH2 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 556,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 557, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 558; and

the VL2 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 559,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 560, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 561; or

b) the VH2 comprises

a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 86,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 557, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 558; and

the VL2 comprises

a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 559,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 560, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 561.

3052. The multispecific antibody of claim 2951, wherein the VH2 comprises the amino acid sequence of SEQ ID NO: 562, and the VL2 comprises the amino acid sequence of SEQ ID NO: 563.

3153. The multispecific antibody of ~~any one of claims 50-52~~claim 29, comprising:

- a) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 564,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 565, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 567;

- b) a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 564,
a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 565, and
a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 569;
- c) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 567;
- d) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 569;
- e) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 567 without the C-terminal lysine;
- f) a first polypeptide comprising the amino acid sequence of SEQ ID NO: 564,
a second polypeptide comprising the amino acid sequence of SEQ ID NO: 565 without the C-terminal lysine, and
a third polypeptide comprising the amino acid sequence of SEQ ID NO: 569 without the C-terminal lysine.

~~54. The multispecific antibody of any one of claims 1-53, wherein the multispecific antibody comprises an Fc region.~~

~~55. The multispecific antibody of claim 54, wherein the Fc region is of the human IgG1 subclass.~~

~~56. The multispecific antibody of claim 55, wherein the Fc region is of the human IgG4 subclass.~~

~~57. The multispecific antibody of any one of claims 54-56, wherein the Fc region has reduced or no antibody dependent cell cytotoxicity (ADCC) effect and/or reduced or no cross-linking effects.~~

58. — The multispecific antibody of any one of claims 1-57, wherein the multispecific antibody comprises a first CH3 domain and a second CH3 domain, wherein:

- i) — the first CH3 domain comprises a cysteine (C) residue at position 390 and the second CH3 domain comprises a cysteine residue at position 400, or the first CH3 domain comprises a cysteine residue at position 400 and the second CH3 domain comprises a cysteine residue at position 390; or
- ii) — the first CH3 domain comprises a cysteine residue at position 392 and the second CH3 domain comprises a cysteine residue at position 397, or the first CH3 domain comprises a cysteine residue at position 397 and the second CH3 domain comprises a cysteine residue at position 392; or
- iii) — the first CH3 domain comprises a cysteine residue at position 392 and the second CH3 domain comprises a cysteine residue at position 400, or the first CH3 domain comprises a cysteine residue at position 400 and the second CH3 domain comprises a cysteine residue at position 392; and

wherein the amino acid residue numbering is based on EU numbering.

59. — The multispecific antibody of claim 58, wherein:

- i) — the first CH3 domain further comprises a positively charged residue at position 357 and the second CH3 domain further comprises a negatively charged residue at position 351, or the first CH3 domain further comprises a negatively charged residue at position 351 and the second CH3 domain further comprises a positively charged residue at position 357; or
- ii) — the first CH3 domain further comprises a positively charged residue at position 411 and the second CH3 domain further comprises a negatively charged residue at position 370, or the first CH3 domain further comprises a negatively charged residue at position 370 and the second CH3 domain further comprises a positively charged residue at position 411; or
- iii) — the first CH3 domain further comprises a positively charged residue at position 364 and the second CH3 domain further comprises a negatively charged residue at position 370, or the first CH3 domain further comprises a negatively charged residue at position 370 and the second CH3 domain further comprises a positively charged residue at position 364; or

a combination of i) and ii), or a combination of i) and iii); and

~~wherein the amino acid residue numbering is based on EU numbering.~~

~~60. The multispecific antibody of claim 59, wherein the first CH3 domain comprises D356K, E357K, S364K and S400C substitutions and the second CH3 domain comprises L351D, K370D, N390C and K439D substitutions, or the first CH3 domain comprises L351D, K370D, N390C and K439D substitutions and the second CH3 domain comprises D356K, E357K, S364K and S400C substitutions.~~

~~61. The multispecific antibody of any one of claims 1-60, wherein the multispecific antibody is a bispecific antibody.~~

~~62. An isolated antibody or antigen binding fragment thereof that specifically binds CD3, comprising:~~

~~a) a VH comprising~~

~~a CDR-H1 comprising an amino acid sequence according to Formula (I): $X_1YAX_2X_3$ (SEQ ID NO: 382), wherein X_1 is D, S, or T, X_2 is I, L, or M, and X_3 is N or T,~~

~~a CDR-H2 comprising an amino acid sequence according to Formula (II):~~

~~RIRSKYNNYATYYAX₁X₂VKX₃ (SEQ ID NO: 383), wherein X_1 is D or E, X_2 is S or T, and X_3 is D, G, or S, and~~

~~a CDR-H3 comprising an amino acid sequence according to Formula (III):~~

~~HGNX₁GX₂SYVSX₃X₄AY (SEQ ID NO: 384), wherein X_1 is F or Y, X_2 is N or T, X_3 is W or Y, and X_4 is F or W; and~~

~~b) a VL comprising~~

~~a CDR-L1 comprising an amino acid sequence according to Formula (IV):~~

~~X₁SSTGAVTX₂X₃NYX₄N (SEQ ID NO: 385), wherein X_1 is A, G, or R, X_2 is S or T, X_3 is G or S, and X_4 is A, P, or V,~~

~~a CDR-L2 comprising an amino acid sequence according to Formula (V):~~

~~GTX₁X₂RAP (SEQ ID NO: 386), wherein X_1 is K or N, and X_2 is F or K, and~~

~~a CDR-L3 comprising an amino acid sequence according to Formula (VI):~~

~~ALWYSX₁X₂WV (SEQ ID NO: 387), wherein X_1 is D, N, or T, and X_2 is L or R.~~

~~63. The isolated antibody or antigen binding fragment thereof of claim 62, wherein:~~

~~a) the VH comprises~~

- ~~a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376, 390, 601, and 602, or a variant thereof comprising up to about 3 amino acid substitutions,~~
 - ~~a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 377, 391-394, and 603, or a variant thereof comprising up to about 3 amino acid substitutions, and~~
 - ~~a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378, 395, 604, and 605, or a variant thereof comprising up to about 3 amino acid substitutions; and~~
 - ~~b) the VL comprises~~
 - ~~a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396-398, and 606-609, or a variant thereof comprising up to about 3 amino acid substitutions,~~
 - ~~a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, or a variant thereof comprising up to about 3 amino acid substitutions, and~~
 - ~~a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, 400-401, or a variant thereof comprising up to about 3 amino acid substitutions, and 610.~~
64. ~~The isolated antibody or antigen binding fragment thereof of claim 62, wherein:~~
- ~~a) the VH comprises~~
 - ~~a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376 and 390,~~
 - ~~a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 391-394, and~~
 - ~~a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378 and 395; and~~
 - ~~b) the VL comprises~~
 - ~~a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396-398,~~

- ~~a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, and~~
- ~~a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, and 400-401.~~
65. ~~The isolated antibody or antigen binding fragment thereof of any one of claims 62-64, wherein:~~
- ~~a) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~b) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~
- ~~c) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;~~
- ~~d) the VH comprises~~

- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~e) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;~~
- ~~f) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~
- ~~g) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 398,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 399, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~

h) ~~the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~

i) ~~the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~

j) ~~the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~

k) ~~the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~

- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;
- ~~l) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~m) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381; or~~
- ~~n) the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.~~
66. ~~The isolated antibody or antigen binding fragment thereof of claim 65, wherein:~~
- ~~the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
- ~~the VL comprises~~

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400.
67. — The isolated antibody or antigen-binding fragment thereof of claim 65, wherein:
the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.
68. — The isolated antibody or antigen-binding fragment thereof of any one of claims 62-67,
wherein:
a) — the VH comprises an amino acid sequence according to Formula (VII):
EVQLVESGGGLVX₁PGGSLRLSCAASGFTFX₂X₃YAIX₄WVRQAPGKGLEWVX₅
RIRSKYNNYATYYAX₆SVKX₇RFTISRDX₈SKNTLYLQX₉NSLRAEDTAVYYC
X₁₀RHGNX₁₁GX₁₂SYVSWFAYWGQGLTVTVSS (SEQ ID NO: 388), wherein X₁ is
K or Q, X₂ is N or S, X₃ is S or T, X₄ is H or N, X₅ is G or S, X₆ is D or E, X₇ is D or
G, X₈ is D or N, X₉ is I or L, X₁₀ is A or V, X₁₁ is F or Y, X₁₂ is N or T; and
b) — the VL comprises an amino acid sequence according to Formula (VIII):
X₁AVVTQEPSLTVSPGGTVTLTCX₂SSTGAVTTSNYX₃NWX₄QKPGQAPRGLI
GGTX₅X₆RAPGX₇PARFSGSLLGGKAALTLSGAQPEDEAEYYCALWYSX₈X₉W
VFGGGTKLTVL (SEQ ID NO: 389), wherein X₁ is E or Q, X₂ is A, G, P, or R, X₃ is
A or P, X₄ is F or V, X₅ is K or N, X₆ is F or K, X₇ is A, I, T, or V, X₈ is A, D, N, or
T, and X₉ is H or L.
69. — The isolated antibody or antigen-binding fragment thereof of any one of claims 62-68,
wherein the VH comprises an amino acid sequence selected from the group consisting of SEQ
ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640, or a variant thereof having at
least about 80% sequence identity to an amino acid sequence selected from the group consisting
of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640; and the VL comprises

~~an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666, or a variant thereof having at least about 80% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666.~~

~~70. The isolated antibody or antigen binding fragment thereof of any one of claims 62-68, wherein the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 402, 405, 407, 409, 410, 412, 414, 415, and 416; and the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 403, 404, 406, 408, 411, and 413.~~

~~71. The isolated antibody or antigen binding fragment thereof of any one of claims 62-70, wherein:~~

- ~~a) the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 403;~~
- ~~b) the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 404;~~
- ~~c) the VH comprises the amino acid sequence of SEQ ID NO: 405, and the VL comprises the amino acid sequence of SEQ ID NO: 406;~~
- ~~d) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 404;~~
- ~~e) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 403;~~
- ~~f) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 408;~~
- ~~g) the VH comprises the amino acid sequence of SEQ ID NO: 409, and the VL comprises the amino acid sequence of SEQ ID NO: 408;~~
- ~~h) the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 411;~~
- ~~i) the VH comprises the amino acid sequence of SEQ ID NO: 412, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~
- ~~j) the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~

- k) ~~the VH comprises the amino acid sequence of SEQ ID NO: 414, and the VL comprises the amino acid sequence of SEQ ID NO: 403;~~
- l) ~~the VH comprises the amino acid sequence of SEQ ID NO: 415, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~
- m) ~~the VH comprises the amino acid sequence of SEQ ID NO: 416, and the VL comprises the amino acid sequence of SEQ ID NO: 413; or~~
- n) ~~the VH comprises the amino acid sequence of SEQ ID NO: 416, and the VL comprises the amino acid sequence of SEQ ID NO: 411.~~

~~72. The isolated antibody or antigen binding fragment thereof of claim 71, wherein the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 403.~~

~~73. The isolated antibody or antigen binding fragment thereof of claim 71, wherein the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 411.~~

~~74. The isolated antibody or antigen binding fragment thereof of any one of claims 62-73, further comprising a second antigen binding fragment that specifically binds a target antigen.~~

~~75. The isolated antibody or antigen binding fragment thereof of claim 74, wherein the target antigen is a tumor antigen.~~

~~76. The isolated antibody or antigen binding fragment thereof of claim 75, wherein the tumor antigen is HER2, CD20, TROP2, BCMA, or CD19.~~

~~77. A masked antibody, comprising a masking moiety (MM) and an antibody or antigen binding fragment that binds CD3, wherein the antibody or antigen binding fragment comprises a VH and a VL;~~

~~wherein the masked antibody comprises a single polypeptide chain and the VH and the VL of the antibody or antigen binding fragment are part of the single polypeptide chain, or the masked antibody comprises two polypeptide chains, and the VH and the VL of the antibody or antigen binding fragment are part of different polypeptide chains of the masked antibody;~~

~~— wherein the C terminus of the MM is fused to the N terminus of the VH or the VL of the antibody or antigen binding fragment;~~

~~wherein the MM competes with CD3 to specifically bind the antibody or antigen binding fragment; and~~

wherein the antibody or antigen binding fragment binds CD3 with half maximal binding at a concentration of antibody (EC_{50}) that is at least 10 nM as determined by an enzyme-linked immunosorbent assay (ELISA).

78. — The masked antibody of claim 77, wherein the MM comprises:

a) the amino acid sequence of EVGSY (SEQ ID NO: 667) at the N-terminus of the MM;
or

b) an amino acid sequence according to Formula (IX): PYDDPDCPSHX₁SDCDX₂ (SEQ ID NO: 668), wherein X₁ is D or E, and X₂ is N or Q.

79. — The masked antibody of claim 78, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, and 597-599.

80. — The masked antibody of claim 79, wherein the MM comprises the amino acid sequence of SEQ ID NO: 417.

81. A masked antibody comprising a masking moiety (MM) and an antibody or antigen binding fragment that binds CD3, wherein the antibody or antigen binding fragment comprises a VH and a VL;

wherein the masked antibody comprises a single polypeptide chain and the VH and the VL of the antibody or antigen binding fragment are part of the single polypeptide chain, or the masked antibody comprises two polypeptide chains, and the VH and the VL of the antibody or antigen binding fragment are part of different polypeptide chains of the masked antibody;

— wherein the C-terminus of the MM is fused to the N-terminus of the VH or the VL of the antibody or antigen binding fragment;

wherein the MM competes with CD3 to specifically bind the antibody or antigen binding fragment; and

wherein the MM comprises:—

a) the amino acid sequence of EVGSY (SEQ ID NO: 667) at the N-terminus of the MM;

b) an amino acid sequence according to Formula (IX): PYDDPDCPSHX₁SDCDX₂ (SEQ ID NO: 668), wherein X₁ is D or E, and X₂ is N or Q; or

c) an amino acid sequence according to Formula (X):

X₁X₂X₃DX₄X₅CX₆X₇DX₈X₉X₁₀CX₁₁X₁₂ (SEQ ID NO: 669), wherein X₁ is A or D, X₂ is A, D, or P, X₃ is D, H, or P, X₄ is F or P, X₅ is D or P, X₆ is D or P, X₇ is A or P, X₈ is D, N, or P, X₉ is A, N, or P, X₁₀ is D, H, or S, X₁₁ is H, P, or Y, and X₁₂ is N, P, or Y.

~~82. The masked antibody of claim 81, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, 585-588, and 597-599.~~

~~83. The masked antibody of any one of claims 77-82, wherein the antibody or antigen-binding fragment comprises an anti-CD3 antigen-binding fragment selected from the group consisting of a Fab, a Fv, a scFab and a scFv.~~

~~84. The masked antibody of claim 83, wherein the antibody or antigen-binding fragment is a scFv comprising from the N-terminus to the C-terminus, the VL, a linker and the VH.~~

~~85. The masked antibody of any one of claims 77-84, wherein the masked antibody comprises an amino acid linker between the C-terminus of the MM and the N-terminus of the VH or the VL of the antibody or antigen-binding fragment.~~

~~86. The masked antibody of any one of claims 77-85, wherein the masked antibody further comprises a cleavable linker.~~

~~87. The masked antibody of claim 86, wherein the cleavable linker is between the C-terminus of the MM and the N-terminus of the VH or the VL of the antibody or antigen-binding fragment.~~

~~88. The masked antibody of any one of claims 77-85, wherein the masked antibody does not comprise a cleavable linker.~~

~~89. The masked antibody of any one of claims 77-88, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 35, 417, and 597-599, and wherein:~~

~~a) the VH comprises~~

~~a CDR-H1 comprising an amino acid sequence according to Formula (I): $X_1YAX_2X_3$ (SEQ ID NO: 382), wherein X_1 is D, S, or T, X_2 is I, L, or M, and X_3 is N or T;~~

~~a CDR-H2 comprising an amino acid sequence according to Formula (II):~~

~~$RIRSKYNNYATYYAX_1X_2VKX_3$ (SEQ ID NO: 383), wherein X_1 is D or E, X_2 is S or T, and X_3 is D, G, or S, and~~

~~a CDR-H3 comprising an amino acid sequence according to Formula (III):~~

~~$HGNX_1GX_2SYVSX_3X_4AY$ (SEQ ID NO: 384), wherein X_1 is F or Y, X_2 is N or T, X_3 is W or Y, and X_4 is F or W; and~~

~~b) the VL comprises~~

~~a CDR-L1 comprising an amino acid sequence according to Formula (IV):~~

~~X₁SSTGAVTX₂X₃NYX₄N (SEQ ID NO: 385), wherein X₁ is A, G, or R, X₂ is S or T, X₃ is G or S, and X₄ is A, P, or V,~~

~~a CDR-L2 comprising an amino acid sequence according to Formula (V):~~

~~GTX₁X₂RAP (SEQ ID NO: 386), wherein X₁ is K or N, and X₂ is F or K, and~~

~~a CDR-L3 comprising an amino acid sequence according to Formula (VI):~~

~~ALWYSX₁X₂WV (SEQ ID NO: 387), wherein X₁ is D, N, or T, and X₂ is L or R.~~

90. ~~—The masked antibody of claim 89, wherein:~~

~~a) the VH1 comprises~~

~~a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376, 390, 601, and 602, or a variant thereof comprising up to about 3 amino acid substitutions,~~

~~a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 377, 391-394, and 603, or a variant thereof comprising up to about 3 amino acid substitutions, and~~

~~a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378, 395, 604, and 605, or a variant thereof comprising up to about 3 amino acid substitutions; and~~

~~b) the VL1 comprises~~

~~a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396-398, and 606-609, or a variant thereof comprising up to about 3 amino acid substitutions,~~

~~a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, or a variant thereof comprising up to about 3 amino acid substitutions, and~~

~~a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, 400-401, and 610, or a variant thereof comprising up to about 3 amino acid substitutions.~~

91. ~~—The masked antibody of claim 90, wherein:~~

~~a) the VH comprises~~

- ~~a CDR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 376 and 390,~~
- ~~a CDR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 391-394, and~~
- ~~a CDR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 378 and 395; and~~
- ~~b) the VL comprises~~
 - ~~a CDR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 396-398,~~
 - ~~a CDR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 380 and 399, and~~
 - ~~a CDR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 381, and 400-401.~~

92. — ~~The masked antibody of claim 91, wherein:~~

- ~~a) the VH comprises~~
 - ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,~~
 - ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
 - ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
 - ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
 - ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
 - ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~b) the VH comprises~~
 - ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
 - ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and~~
 - ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
- ~~the VL comprises~~
 - ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
 - ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
 - ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~
- ~~c) the VH comprises~~

- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;~~
- ~~d) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- ~~e) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 401;~~
- ~~f) the VH comprises
a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and
the VL comprises
a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~

~~g) the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 398,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 399, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~

~~h) the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~

~~i) the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~

~~j) the VH comprises~~

~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,
a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and
a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~

~~the VL comprises~~

~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,
a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~

- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;
- k) ~~the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 376,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400;~~
- l) ~~the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 393, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381;~~
- m) ~~the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 396,~~
- ~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
- ~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381; or~~
- n) ~~the VH comprises~~
- ~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
- ~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 391, and~~
- ~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 378; and~~
- ~~the VL comprises~~
- ~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~

- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and
a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.
93. ~~The masked antibody of claim 92, wherein:~~
~~the VH comprises~~
~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 392, and~~
~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
~~the VL comprises~~
~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 400.~~
94. ~~The masked antibody of claim 92, wherein:~~
~~the VH comprises~~
~~a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390,~~
~~a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and~~
~~a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and~~
~~the VL comprises~~
~~a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397,~~
~~a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and~~
~~a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.~~
95. ~~The masked antibody of any one of claims 77-94, wherein:~~
a) ~~the VH comprises an amino acid sequence according to Formula (VII):~~
~~EVQLVESGGGLVX₁PGGSLRLSCAASGFTFX₂X₃YAIX₄WVRQAPGKGLEWVX₅~~
~~RIRSKYNNYATYYAX₆SVKX₇RFTISRDX₈SKNTLYLQX₉NSLRAEDTAVYYC~~
~~X₁₀RHGNX₁₁GX₁₂SYVSWFAYWGQGLTVTVSS (SEQ ID NO: 388), wherein X₁ is~~
~~K or Q, X₂ is N or S, X₃ is S or T, X₄ is H or N, X₅ is G or S, X₆ is D or E, X₇ is D or~~
~~G, X₈ is D or N, X₉ is I or L, X₁₀ is A or V, X₁₁ is F or Y, X₁₂ is N or T; and~~
b) ~~the VL comprises an amino acid sequence according to Formula (VIII):~~
~~X₁AVVTQEPSLTVSPGGTVTLTCX₂SSTGAVTTSNYX₃NWX₄QQKPGQAPRGLI~~
~~GGTX₅X₆RAPGX₇PARFSGSLLGGKAALTLGAQPEDEAEYYCALWYSX₈X₉W~~
~~VFGGGTKLTVL (SEQ ID NO: 389), wherein X₁ is E or Q, X₂ is A, G, P, or R, X₃ is~~

A or P, X₄ is F or V, X₅ is K or N, X₆ is F or K, X₇ is A, I, T, or V, X₈ is A, D, N, or T, and X₉ is H or L.

96. — The masked antibody of claim 95, wherein the VH1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640, or a variant thereof having at least about 80% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 67, 402, 405, 407, 409, 410, 412, 414-416, and 611-640; and the VL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666, or a variant thereof having at least about 80% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs: 68, 403, 404, 406, 408, 411, 413, and 641-666.

97. — The masked antibody of claim 95, wherein the VH comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 402, 405, 407, 409, 410, 412, 414, 415, and 416; and the VL comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 403, 404, 406, 408, 411, and 413.

98. — The masked antibody of claim 97, wherein the antibody or antigen-binding fragment comprises:

wherein:

- a) the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 403;
- b) the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 404;
- c) the VH comprises the amino acid sequence of SEQ ID NO: 405, and the VL comprises the amino acid sequence of SEQ ID NO: 406;
- d) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 404;
- e) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 403;
- f) the VH comprises the amino acid sequence of SEQ ID NO: 407, and the VL comprises the amino acid sequence of SEQ ID NO: 408;
- g) the VH comprises the amino acid sequence of SEQ ID NO: 409, and the VL comprises the amino acid sequence of SEQ ID NO: 408;

- h) ~~the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 411;~~
- i) ~~the VH comprises the amino acid sequence of SEQ ID NO: 412, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~
- j) ~~the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~
- k) ~~the VH comprises the amino acid sequence of SEQ ID NO: 414, and the VL comprises the amino acid sequence of SEQ ID NO: 403;~~
- l) ~~the VH comprises the amino acid sequence of SEQ ID NO: 415, and the VL comprises the amino acid sequence of SEQ ID NO: 413;~~
- m) ~~the VH comprises the amino acid sequence of SEQ ID NO: 416, and the VL comprises the amino acid sequence of SEQ ID NO: 413; or~~
- n) ~~the VH comprises the amino acid sequence of SEQ ID NO: 416, and the VL comprises the amino acid sequence of SEQ ID NO: 411.~~

99. ~~The masked antibody of claim 98, wherein the VH comprises the amino acid sequence of SEQ ID NO: 402, and the VL comprises the amino acid sequence of SEQ ID NO: 403.~~

100. ~~The masked antibody of claim 98, wherein the VH comprises the amino acid sequence of SEQ ID NO: 410, and the VL comprises the amino acid sequence of SEQ ID NO: 411.~~

101. ~~The masked antibody of any one of claims 77-100, wherein the antibody or antigen-binding fragment comprises the amino acid sequence of SEQ ID NO: 421 or SEQ ID NO: 422.~~

102. ~~The masked antibody of any one of claims 77-101, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 585-588, and wherein the VH comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 368, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 369, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 370; and the VL comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 371, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 372, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 373.~~

103. ~~The masked antibody of claim 102, wherein the VH comprising the amino acid sequence of SEQ ID NO: 366, and the VL comprising the amino acid sequence of SEQ ID NO: 367.~~

~~104.— The masked antibody of any one of claims 77-103, comprising, from N-terminus to C-terminus, the masking moiety (MM), a cleavable moiety (CM), and the antibody or antigen-binding fragment,~~

~~wherein the CM comprises a cleavage site;~~

~~wherein the MM inhibits binding of the masked antibody to CD3 when the CM is not cleaved; and~~

~~wherein the masked antibody binds CD3 via the VH and the VL when the CM is cleaved.~~

~~105.— The masked antibody of claim 104, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431 and 477-490, and 516-555.~~

~~106.— The masked antibody of claim 105, wherein the CM comprises the amino acid sequence of SEQ ID NO: 77 or 418.~~

~~107.— The masked antibody of any one of claims 77-103, comprising, from N-terminus to C-terminus, the masking moiety (MM), a non-cleavable linker (NCL), and the antibody or antigen-binding fragment.~~

~~108.— A masked antibody, comprising a masking moiety (MM) and an antibody or antigen-binding fragment that binds HER2, wherein the antibody or antigen-binding fragment comprises a VH and a VL;~~

~~wherein the masked antibody comprises a single polypeptide chain and the VH and the VL of the antibody or antigen-binding fragment are part of the single polypeptide chain, or the masked antibody comprises two polypeptide chains, and the VH and the VL of the antibody or antigen-binding fragment are part of different polypeptide chains of the masked antibody;~~

~~— wherein the C-terminus of the MM is fused to the N-terminus of the VH or the VL of the antibody or antigen-binding fragment;~~

~~wherein the MM competes with HER2 to specifically bind the antibody or antigen-binding fragment; and~~

~~wherein the masked antibody binds HER2 via the VH and VL, and wherein the MM comprises:~~

~~a) an amino acid sequence according to Formula (XI): ESX₁X₂CX₃X₄DPFX₅CQX₆ (SEQ ID NO: 670), wherein X₁ is D or E, X₂ is A, F, V, or Y, X₃ is D or E, X₄ is A or L, X₅ is D or E, and X₆ is A, F, or Y;~~

- b) an amino acid sequence according to Formula (XII): $X_1X_2X_3X_4X_5X_6CX_7X_8DPYECX_9X_{10}$ (SEQ ID NO: 671), wherein X_1 is A, H, or S, X_2 is A, D, or S, X_3 is A, T, or V, X_4 is P, S, or T, X_5 is D or E, X_6 is A or V, X_7 is D or E, X_8 is A or L, X_9 is Q, S, or T, and X_{10} is A, H, or V; or
- c) an amino acid sequence according to Formula (XIII): $YNSDDDCX_1SX_2YDPYTCYY$ (SEQ ID NO: 672), wherein X_1 is A, I, or V, and X_2 is H or R.

109. — The masked antibody of claim 108, comprising, from N terminus to C terminus, the masking moiety (MM), a cleavable moiety (CM), and the antibody or antigen binding fragment, wherein the CM comprises a cleavage site; wherein the MM inhibits binding of the masked antibody to HER2 when the CM is not cleaved; and wherein the masked antibody binds HER2 via the VH and VL when the CM is cleaved.

110. — The masked antibody of claim 108 or claim 109, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 36, 419, 432-476, and 491-515.

111. — The masked antibody of claim 108 or claim 109, wherein the CM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 77, 127-129, 418, 420, 431 and 477-490, and 516-555.

112. — The masked antibody of any one of claims 108-111, wherein the VH comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 423, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 424, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 71, and the VL comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 72, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 73, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 74.

113. — The masked antibody of any one of claims 108-112, wherein the VH comprises the amino acid sequence of SEQ ID NO: 75, and the VL comprises the amino acid sequence of SEQ ID NO: 76.

114. — The masked antibody of any one of claims 108-113, wherein the masked antibody comprises an amino acid linker between the C terminus of the MM and the N terminus of the VH or the VL of the antibody or antigen binding fragment.

115. — The masked antibody of any one of claims 108-114, wherein the masked antibody further comprises a cleavable linker.

~~116. — The masked antibody of claim 115, wherein the cleavable linker is between the C-terminus of the MM and the N-terminus of the VH or the VL of the antibody or antigen-binding fragment.~~

~~117. — The masked antibody of any one of claims 108–114, wherein the masked antibody does not comprise a cleavable linker.~~

~~118. — One or more isolated nucleic acids encoding the multispecific antibody, isolated antibody or antigen-binding fragment thereof, or masked antibody of any one of claims 1–117.~~

~~119. — A vector comprising the one or more nucleic acids of claim 118.~~

~~120. — A host cell comprising the one or more nucleic acids of claim 118 or the vector of claim 119.~~

~~121. — A method for preparing a multispecific antibody, an isolated antibody or antigen-binding fragment thereof, or a masked antibody, comprising:~~

- ~~a) culturing the host cell of claim 120 under conditions that allow expression of the one or more nucleic acids or vector; and~~
- ~~b) recovering the multispecific antibody, the antibody or antigen-binding fragment thereof, or the masked antibody from the host cell culture.~~

~~122. — A pharmaceutical composition comprising the multispecific antibody, isolated antibody or antigen-binding fragment thereof, or masked antibody of any one of claims 1–117, and a pharmaceutically acceptable carrier.~~

~~123. — A method for treating a disease or condition in a subject in need thereof, comprising administering to the subject an effective amount of the pharmaceutical composition of claim 122.~~

~~124. — The method of claim 123, wherein the disease or condition is cancer.~~

~~125. — The method of claim 124, wherein the target antigen is HER2, and wherein the cancer is selected from the group consisting of breast cancer, ovarian cancer, and lung cancer.~~

~~126. — The method of claim 124, wherein the target antigen is CD20, and wherein the cancer is lymphoma or leukemia.~~

~~127. — The method of claim 124, wherein the target antigen is TROP2, and wherein the cancer is breast cancer or lymphoma.~~

~~128. — The method of any one of claims 123–127, wherein the pharmaceutical composition is administered such that the multispecific antibody, isolated antibody or antigen-binding fragment~~

thereof, or masked antibody is provided to the subject at a dose of 0.02mg/kg, 0.2mg/kg, 2mg/kg, 10mg/kg, 30mg/kg, or 60mg/kg.

129. — The method of claim 128, wherein the multispecific antibody, isolated antibody or antigen-binding fragment thereof, or masked antibody comprises:

a) — a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 427,

a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 428, and

a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 112;

b) — a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 83,

a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 84, and

a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 85;

c) — a first polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 683,

a second polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 684, and

a third polypeptide comprising an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 685;

d) — a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 112;

e) — a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85;

f) — a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685;

g) —a first polypeptide comprising the amino acid sequence of SEQ ID NO: 427 without the C-terminal lysine,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 428 without the C-terminal lysine, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 442;

h) —a first polypeptide comprising the amino acid sequence of SEQ ID NO: 83,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 84 without the C-terminal lysine, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 85 without the C-terminal lysine; or

i) —a first polypeptide comprising the amino acid sequence of SEQ ID NO: 683,

a second polypeptide comprising the amino acid sequence of SEQ ID NO: 684 without the C-terminal lysine, and

a third polypeptide comprising the amino acid sequence of SEQ ID NO: 685 without the C-terminal lysine.

130. —The method of any one of claims 123–129, further comprising administering to the subject an anti-PD-1 or anti-PD-L1 antibody.

131. —The method of any one of claims 123–129, further comprising administering to the subject a CD137 agonist or antibody.

132. —The method of claim 131, wherein the CD137 agonist or antibody comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a CDR-H1 comprising the amino acid sequence of TGGVGVG (SEQ ID NO:700), a CDR-H2 comprising the amino acid sequence of LIDWADDKYYSPSLKS (SEQ ID NO:701), and a CDR-H3 comprising the amino acid sequence of GGS DTVIGDWFAY (SEQ ID NO:702); and wherein the light chain variable region comprises a CDR-L1 comprising the amino acid sequence of RASQSIGSYLA (SEQ ID NO:703), a CDR-L2 comprising the amino acid sequence of DASNLET (SEQ ID NO:704), and a CDR-L3 comprising the amino acid sequence of QQGYLWT (SEQ ID NO:705).

133. —The method of claim 132, wherein the heavy chain variable region of the CD137 agonist or antibody comprises the amino acid sequence of SEQ ID NO:706, and wherein the light chain

~~variable region of the CD137 agonist or antibody comprises the amino acid sequence of SEQ ID NO:707.~~

~~134. The method of claim 132 or claim 133, wherein the heavy chain of the CD137 agonist or antibody comprises the amino acid sequence of SEQ ID NO:710, and wherein the light chain of the CD137 agonist or antibody comprises the amino acid sequence of SEQ ID NO:711.~~

32. The multispecific antibody of claim 2, wherein the VH1 comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 390, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 394, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 395; and the VL1 comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 397, a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 380, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 381.

33. The multispecific antibody of claim 32, wherein the ScFv comprises the amino acid sequence of SEQ ID NO: 422.

34. The multispecific antibody of claim 32, wherein the MM1 comprises the amino acid sequence of SEQ ID NO: 417.

35. The multispecific antibody of claim 33, wherein the MM1 comprises the amino acid sequence of SEQ ID NO: 417.

36. The multispecific antibody of claim 34, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 77.

37. The multispecific antibody of claim 35, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 77.

38. The multispecific antibody of claim 34, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 418.

39. The multispecific antibody of claim 35, wherein the CM1 comprises the amino acid sequence of SEQ ID NO: 418.

40. The multispecific antibody of claim 3, wherein the second polypeptide has the amino acid sequence of SEQ ID NO: 567.

41. The multispecific antibody of claim 40, wherein the first polypeptide has the amino acid sequence of SEQ ID NO: 565.

42. The multispecific antibody of claim 41, wherein the third polypeptide has the amino acid sequence of SEQ ID NO: 564.

43. The multispecific antibody of claim 8, wherein the second polypeptide has the amino acid sequence of SEQ ID NO: 85.

44. The multispecific antibody of claim 43, wherein the first polypeptide has the amino acid sequence of SEQ ID NO: 84.

45. The multispecific antibody of claim 44, wherein the third polypeptide has the amino acid sequence of SEQ ID NO: 83.

46. The multispecific antibody of claim 27, comprising:
a first polypeptide having an amino acid sequence of SEQ ID NO: 427,
a second polypeptide having an amino acid sequence of SEQ ID NO: 428, and
a third polypeptide having an amino acid sequence of SEQ ID NO: 112.

47. The multispecific antibody of any one of claim 31, comprising:
a first polypeptide having an amino acid sequence having an amino acid sequence of SEQ ID NO: 564,
a second polypeptide having an amino acid sequence of SEQ ID NO: 565, and
a third polypeptide having an amino acid sequence of SEQ ID NO: 567.